REMARKS

A substitute specification and a marked up specification have been provided to correct typographical errors and to comply with 37 CFR 1.77(b). No new matter has been added.

Claims 1-11 have been canceled. New claims 14-24 have been added to more clearly define the invention.

Claim Objections

Claim 1 has been objected to because of informalities. Claim 1 has been canceled thus rendering the objection moot. Applicants respectfully request that the claim objection be reconsidered and withdrawn.

Claim Rejections under 35 USC §112

Claims 1 and 2 have been rejection under 35 U.S.C. 112, second paragraph, as being indefinite. Claims 1 and 2 have been canceled thus rendering the rejection moot. Applicants respectfully request that the claim rejection under 35 U.S.C..112 be reconsidered and withdrawn.

Claim rejection under 35 USC §102/103

Claims 1, 2, 4 and 5 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Lamberts, 2002, European Journal of Endocrinology, 146, 701-705 as evidenced by Bruns, 2002, The Expanding Role of Ocreotide II: Advances in Endocrinology and Eye Diseases, Eds SWJ Lamberts & e. Ghico, Pages 251-254.

Also, Claims 1-11 are rejected under 35 U.S.C. 103(a) as obvious over Lamberts, 2002, European Journal of Endocrinology, 146, 701-705 as evidenced by Bruns, 2002, The Expanding Role of Ocreotide II: Advances in Endocrinology and Eye Diseases, Eds SWJ Lamberts & e. Ghico, Pages 251-254 in view of US 5,876,761 issued to Bodmer.

Claims 1-11 have been canceled. Applicants respectfully request that the rejections under 35 U.S.C 102/103 be reconsidered and withdrawn.

New claim 14 has been restricted to Compound A following the disclosure on page 4 penultimate paragraph of the description and finds further basis in previous claim 4.

New claims 16 and 17 cover a preferred embodiments defining the polymer matrix according to page 8, third full paragraph of the description. New claim 18 covers a preferred embodiment further defining the preferred particle size of the compound. Further support for the amended and new claims is found in Example 5 to 8. It is submitted that the new claims add no new matter.

Applicant would like to point out to the Examiner that, whereas depot formulations for peptide drugs have been described in the cited prior art, it is still to date challenging to develop sustained release formulations comprising a peptide drug which are suitable for therapeutic uses. For instance, maintaining a therapeutically relevant blood level over an extended period of time is difficult to obtain for a peptide (see e.g. Bodmer et al., US5,876,761, column 1, lines 26 and 27).

The present invention now provides advantageous microparticle compositions comprising Compound A. As described in example 2b, table 4 of the description, microparticles comprising a star shaped polylactide-co-glycolide polymer showed no release over the first 16 days when the particle size of Compound A was small. The problem of this initial low release ("lag-phase") can now be overcome in accordance with the present invention by using a polymer as defined in new claim 14 comprising a star shaped and a linear polylactide-co-glycolide polymer.

The following plasma levels of Compound A were observed in rabbits for microparticles as described in Example 8 of the present application (4mg of Compound A per kg of the rabbit):

Table 1:

Time after administration [days]	0	0.021	0.042	0.083	0.167	0.25	1	2	3	6	9
Microparticles of Example 8	0	12.40	11.51	17.61	17.13	13.09	5.73	4.58	4.58	13.32	9.15
Time after administration [days]	13	16	20	23	27	30	34	37	41	44	49
Microparticles of Example 8	4.82	4.93	6.89	6.22	7.71	3.30	1.39	0.88	0.47	0.0	0.0

Plasma levels of Compound A are determined using an ELISA method. Mean concentration of Compound A after administration is given in Table 1. Mean AUC (0-55 d) is found to be 227 ng/ml d for example 8. Particle size of Compound A: x90 < 4.8 microns.

As clearly demonstrated by Table 1, the microparticles of Example 8 do not have an initial lag-phase.

The cited prior art documents do not mention the problem of initial low release. The skilled person faced with this problem to be solved does not get any hint from the cited prior art alone or in combination in order to come to the solution of the present invention.

Should the Examiner have any questions, please contact the undersigned attorney.

Respectfully submitted,

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